

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No.: KUZ-0018
Inventors: Yasukochi et al.
Serial No.: 10/502,412
Filing Date: July 23, 2004
Examiner: Cheung, William K.
Group Art Unit: 1796
Title: Process for Production of Pressure-
Sensitive Adhesive Moldings
Comprising Closslinked Polymers as
the Main Component

Commissioner for Patents
U.S. Patent & Trademark Office

Dear Sir:

DECLARATION UNDER 37 C.F.R. 1.132

I, Takashi Yasukochi, declare as follows:

1. I am one of the co-inventors of U.S. Application Serial No. 10/502,412 filed on July 23, 2004. I am thoroughly familiar with the contents of said Application, its prosecution before the United States Patent and Trademark Office and the references cited therein.

2. I graduated from the Osaka University with a degree of Science in 1999.

3. I have been employed by Hisamitsu Pharmaceutical

Co. Inc. since 1999, as a Researcher in the Exploratory Research Laboratories.

4. I am thoroughly familiar with the Office Action which was mailed on September 18, 2008 where the Examiner rejected the claimed subject matter as being obvious over the teachings of Kamiyama (WO 99/02141) in view of Matsumoto et al. (US 5,532,373).

5. In order to overcome the rejection, the following experiments were conducted under my control.

6. The experiments herein were conducted in accordance with procedures disclosed in the specification examples.

EXPERIMENTAL REPORT

1.OBJECT

The object of the experiment conducted herein is to confirm that crosslinking of hydroxyl group-containing polymers by boric acid or metal alcolate without using a lower alcohol as solvent cannot produce a matrix type patch formulation with desirable adhesiveness and usability.

2.MATERIALS AND METHODS

(1) Preparation of the formulation with boric acid as the crosslinking agent

i) Crosslinking agent (boric acid) 0.05g and solvent (either methanol or tetrahydrofuran (THF) 1.7g were mixed and stirred for 3 hours. The resulting mixture of the crosslinking agent and the solvent was examined for dissolving state of the crosslinking agent.

ii) According to the Formulations 1 to 3 in Table 1, an acrylic polymer DURO-TAK (No. 387-2287, National Starch and Chemical Co.) and isopropyl myristate are added to the mixture of the crosslinking agent and the solvent prepared according to i), and stirred for 18 hours to give an adhesive mixture .

iii) The mixture produced in ii) was spread out on silicon -treated surface of a polyethylene terephthalate (PET) film (release film) and crosslinked at 100°C for 15 minutes to give an 80 µm adhesive layer. A PET film was laminated thereto as a support, dried at 65°C for 48 hours to give a matrix formulation. Stringiness and plaster residual were examined to assess the adhesive properties of the formulation thus obtained.

Table 1. Adhesive mixtures using boric acid as crosslinking agent

	Formulation 1	Formulation 2	Formulation 3
DURO-TAK 387-2287 (solid content conc. = 50.5%)	4.45 (solid content)	4.45 (solid content)	4.45 (solid content)
isopropyl myristate	0.5g	0.5g	0.5g
boric acid [MeOH solution (30mg/g)]	0.05g		
boric acid [THF solution (30mg/g)]		0.05g	
boric acid [ethyl acetate solution (30mg/g)]			0.05g
total	5.0g	5.0g	5.0g

(2) Preparation of the formulation with metal alcoholate (aluminum isopropoxide) as the crosslinking agent

An adhesive mixture was prepared in a similar manner as (1) but using aluminum isopropoxide as crosslinking agent, according to Formulations 4 to 6 in Table 2, then the dissolving state of the crosslinking agent to the solvent, the nature of the adhesive solution, and the adhesive properties of the resulting formulation were assessed.

Table 2. Adhesive mixtures using aluminum isopropoxide as crosslinking agent

	Formulation 4	Formulation 5	Formulation 6
DURO-TAK 387-2287 (solid content conc. = 50.5%)	4.45 (solid content)	4.45 (solid content)	4.45 (solid content)
isopropyl myristate	5.0g	5.0g	5.0g
aluminum isopropoxide [MeOH solution (30mg/g)]	0.05g		
aluminum isopropoxide [THF solution (30mg/g)]		0.05g	
aluminum isopropoxide			0.05g

[ethyl acetate
solution (30mg/g)]

total	5.0g	5.0g	5.0g
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3.RESULTS

(1) Solubility of crosslinking agent in each solvent

As shown in Table 3, boric acid almost completely dissolved in methanol, but hardly dissolve in Tetrahydrofurane (THF) and ethyl acetate. Aluminum isopropoxide almost dissolved in methanol with small amount of undissolved residual being observed, whereas it hardly dissolve in THF or ethyl acetate.

Table 3. The dissolving state of the crosslinking agent in each solvent

	methanol	THF	ethyl acetate
boric acid	dissolved	hardly dissolved	hardly dissolved
aluminum isopropoxide	a small amount of residual	hardly dissolved	hardly dissolved

(2) The effects of solvent onto the properties of the

formulation

Table 4. Nature of the adhesive mixture

	methanol	THF	ethyl acetate
boric acid	slightly viscous	coagulated (unprocessable)	coagulated (unprocessable)
aluminum isopropoxide	slightly viscous	viscous	viscous

Table 5. Adhesive properties of the formulation

	methanol		THF		ethyl acetate	
	s	p	s	p	s	p
boric acid	no	no	-	-	-	-
aluminum isopropoxide	no	no	yes	yes	yes	yes

s= stringiness, p= plaster residual

The adhesive solution was rendered an appropriate rheology when methanol was used as the solvent of the crosslinking agent, either boric acid or aluminum isopropoxide. The resulting formulation possessed a high cohesiveness, and neither stringiness nor plaster remainings onto the skin was observed.

On the other hand, when THF or ethyl acetate was used as the solvent for boric acid, the adhesive mixture became viscous and coagulated, incapable of being shaped into a sheet. Thus, no assessment of adhesive properties are not available.

When THF or ethyl acetate was used as the solvent of aluminum isopropoxide, the viscosity of the adhesive mixture was increased but the mixture was still capable of being shaped into a sheet. However, the resulting formulation exhibited stringiness when tested by finger tacking functional examination, indicating that the crosslinkage was not sufficiently proceeded.

When these formulation were cut into 2.5cm • (phai) (5cm²), applied to the forearm for two hours and then removed, plaster residuals onto the skin was observed. Further, pain accompanied with the removal, due to the strong adhesion between the formulation and the skin.

CONCLUSION

Accordingly, it was confirmed that the adhesive layer cannot be shaped into a sheet without using lower alcohol as the solvent of the crosslinking agent boric acid or metal alcoholate, or even if a sheet was formed, its adhesive properties and usability is insufficient. Thus, it was confirmed that a uniform formulation having

preferable adhesive properties and usability can be achieved by (1) using a lower alcohol as the solvent for the crosslinkage of hydroxyl group-containing polymers, thereby suppressing the proceeding of crosslinking, then (2) removing the solvent by heating and drying, thereby promoting the proceeding of crosslinking.

4. FIGURES

Figure 1: Photograph showing the mixture of the indicated crosslinking agent (c) and solvent (s).

Photo 1-A: (c)=boric acid, (s)=methanol

Photo 1-B: (c)=boric acid, (s)=THF

Photo 1-C: (c)=boric acid, (s)=ethyl acetate

Figure 2: Photograph showing the mixture of the indicated crosslinking agent (c) and solvent (s).

Photo 1-A: (c)= aluminum isopropoxide, (s)=methanol

Photo 1-B: (c)= aluminum isopropoxide, (s)=THF

Photo 1-C: (c)= aluminum isopropoxide, (s)=ethyl
acetate

Figure 1.

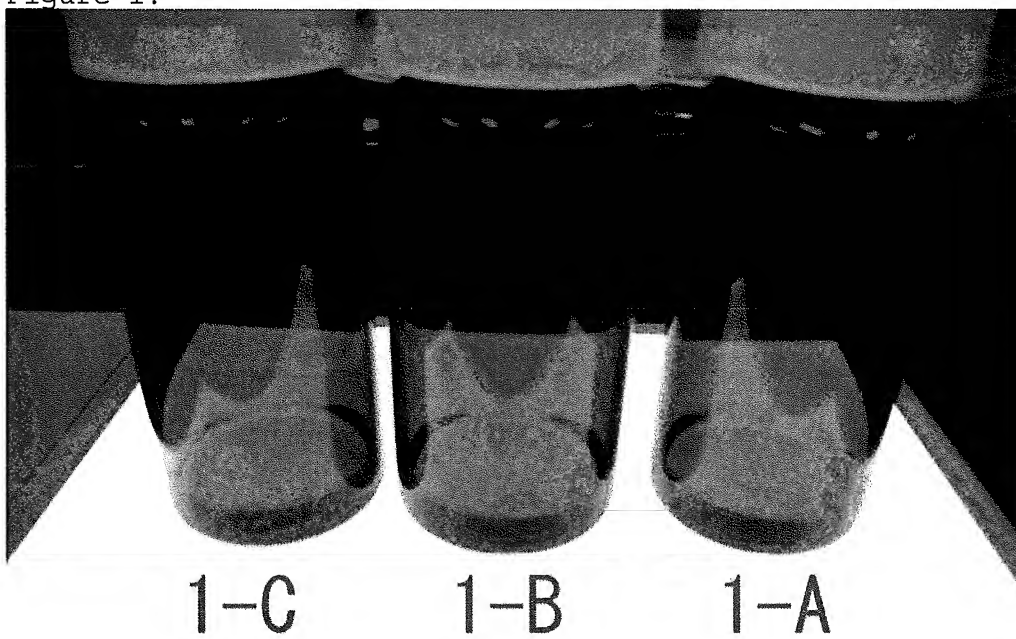
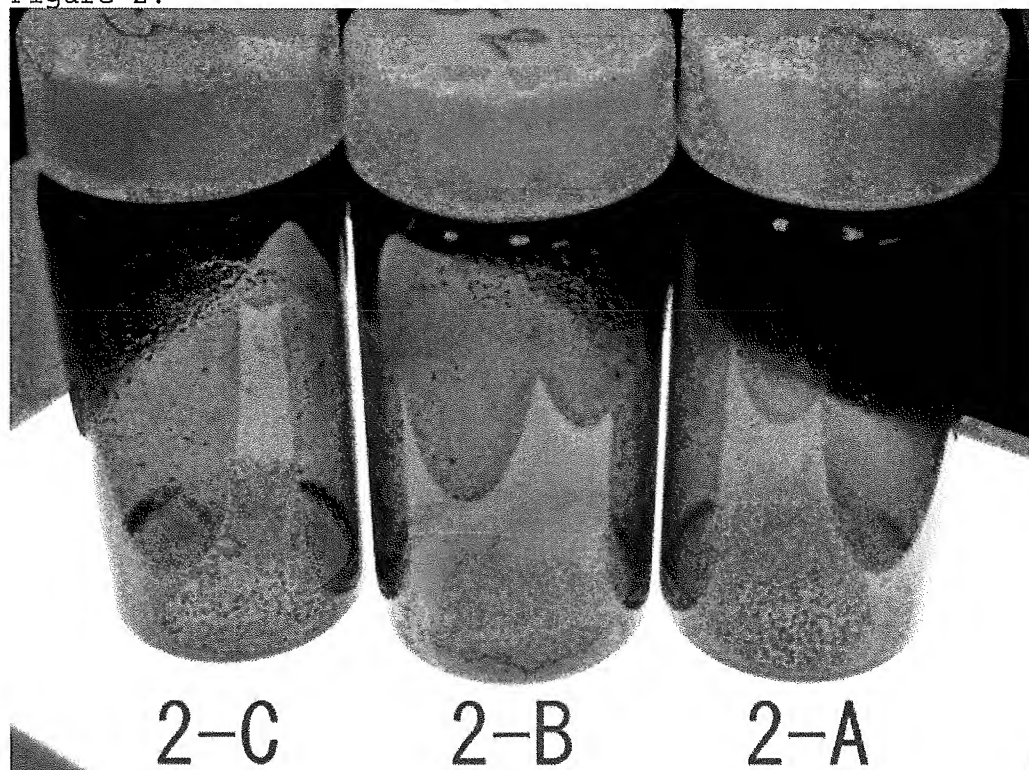


Figure 2.



I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dec 17, 2008

Date

Takashi Yasukochi

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